

WHAT IS CLAIMED IS:

1. A substantially hydrophilic conjugate comprising a peptide covalently linked to a water-soluble, nonpeptidic polymer, wherein said peptide is stabilized in circulation and said conjugate can transport across the blood-brain barrier of a mammal.
- 5 2. The conjugate of Claim 1 wherein said peptide is an analgesic peptide selected from the group consisting of dynorphins, enkephalins, double enkephalins, endorphins, endomorphins, and analogs and derivatives thereof.
- 10 3. The conjugate of Claim 2, wherein said peptide is selected from the group consisting of Met-enkephalin, Leu-enkephalin, endomorphin I, endomorphin II, and analogs or dimeric forms thereof.
4. The conjugate of Claim 2, wherein said peptide is dynorphin A or fragments thereof.
5. The conjugate of Claim 2, wherein said peptide is biphalin.
6. The conjugate of Claim 2, wherein said peptide is DPDPE.
- 15 7. The conjugate of Claim 1, wherein said water-soluble, nonpeptidic polymer is polyethylene glycol or a copolymer of polyethylene glycol and polypropylene glycol.
8. The conjugate of Claim 1, wherein said water-soluble, nonpeptidic polymer is polyethylene glycol.
- 20 9. The conjugate of Claim 8, wherein said polyethylene glycol is selected from the group consisting of monomethoxypolyethylene glycol, branched polyethylene glycol, polyethylene glycol with degradable linkages in the backbone, homobifunctional polyethylene glycol, heterobifunctional polyethylene glycol, multi-arm polyethylene glycol, pendant polyethylene glycol, and forked polyethylene glycol.

10. The conjugate of Claim 9, wherein said peptide is conjugated to at least one polyethylene glycol molecule.

11. The conjugate of Claim 3, wherein the dimeric form of said peptide has two polyethylene glycol chains covalently attached.

5 12. The conjugate of Claim 5, wherein said biphalin has two polyethylene glycol chains covalently attached.

13. The conjugate of Claim 8, wherein said polyethylene glycol has a nominal average molecular weight of about 200 daltons to about 100,000 daltons.

10 14. The conjugate of Claim 13, wherein said polyethylene glycol has a nominal average molecular weight of about 1000 daltons to about 40,000 daltons.

15. The conjugate of Claim 13, wherein said polyethylene glycol has a nominal average molecular weight of 2000 daltons.

16. A composition comprising a conjugate according to Claim 1 and a pharmaceutically acceptable carrier for said conjugate.

15 17. A method for delivering a peptide into the brain of an animal through the blood-brain barrier comprising:

providing a conjugate between a peptide and a water-soluble polymer, non-peptidic polymer;

20 administering said conjugate into the blood stream of an animal; and transporting the conjugate across the blood-brain barrier of said animal.

18. The method of Claim 18, wherein said peptide is an analgesic peptide.

19. The method of Claim 18, wherein said polymer is selected from the group consisting of copolymers of polyethylene glycol and polypropylene glycol, monomethoxypolyethylene glycol, branched polyethylene glycol, polyethylene glycol with degradable linkages in the backbone, homobifunctional polyethylene glycol,

~~heterobifunctional polyethylene glycol, multi-arm polyethylene glycol, pendant polyethylene glycol, and forked polyethylene glycol.~~

20. The method of Claim 19, wherein said polyethylene glycol has a nominal average molecular weight from about 200 to about 100,000 daltons.

5 21. The method of Claim 18, wherein said peptide is an analgesic peptide selected from the group consisting of dynorphins, enkephalins, endorphins, endomorphins, biphalin, and analogs and derivatives thereof.

22. The method of Claim 17, wherein said peptide is conjugated to at least one polymer molecule.

10 23. The method of Claim 17, wherein said peptide is conjugated to at least two polymer molecules.

24. The method of Claim 17, wherein said step of administering said conjugate comprises parenterally injecting said conjugate into said animal.

15 25. The method of Claim 17, wherein said step of administering said conjugate comprises of pulmonary and intranasal inhalation into said animal.

26. The method of Claim 17, wherein said step of administering said conjugate is by oral, ocular, buccal, transdermal, or rectal administration.

27. A method for delivering into the brain of an animal through the blood-brain barrier an agent that is incapable of crossing the blood-brain barrier comprising:

20 providing a conjugate comprising a water-soluble, nonpeptidic polymer, a peptide that is transportable across the blood-brain barrier covalently linked to said polymer, and a nontransportable agent also covalently linked to the polymer; and

administering the conjugate into the blood stream of said animal and transporting the conjugate across the blood-brain barrier of said animal.

25 28. The method of Claim 27, wherein said non-transportable agent is an imaging agent.

29. The method of Claim 27, wherein said non-transportable agent is doxorubicin.

odd
a + 1
x 2